“Polio Immunization: Moving Forward”

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Introduction to OPV Roundtable

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Proposed issues for discussion:

When is OPV efficacious and when is it not?

What is the reason for vaccine-associated poliomyelitis - vaccine reversion or exceptional host susceptibility?

Do evolved OPV derivatives (VDPVs) significantly differ phenotypically from wild polioviruses?

What is the nature of cryptic circulation of VDPV?

Under what conditions, and why, is OPV dangerous?

Background:

(i) OPV viruses have inherited many properties of their parental wild polioviruses

(ii) Wild polioviruses cause paralytic poliomyelitis in one out of several hundred infected non-immune persons

Hence, they are highly attenuated pathogens

They exhibit variable levels of pathogenicity

(iii) There is no evidence that clinical cases of polio caused by wild viruses are due to exceptionally pathogenic viral variants

Hence, increased host susceptibility seems to be the major factor responsible for development of the disease

Background:

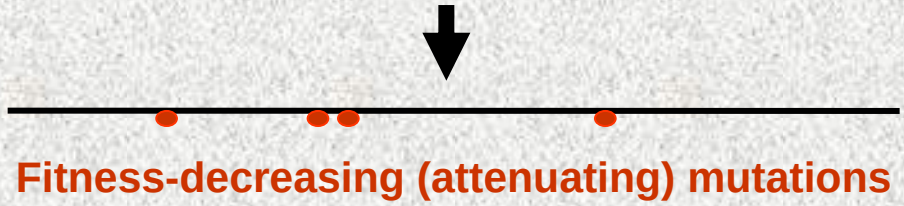
(iv) Albert Sabin had selected from wild polioviruses much more attenuated variants

Selection of OPV:

Passages in non-natural hosts and cells

Multiple plaque cloning – picking-up non-representative variants from heterogeneous viral populations

Deliberate selection of attenuated (= less fit) variants



Fitness-decreasing (attenuating) mutations

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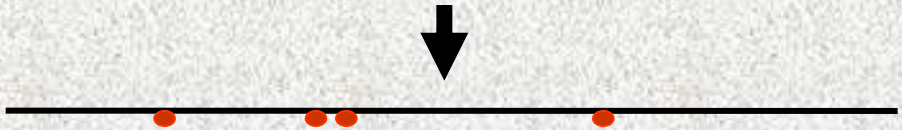

Fitness-decreasing (attenuating) mutations

Being less fit, OPV strains are several-orders-of-magnitude more attenuated - cause poliomyelitis in *one per ~10^6* infected

(likely, due to exceptional susceptibility of the victims)

This makes OPV a very efficacious and reasonably safe vaccine

Background:

(v) However, fitness-decreasing attenuation mutations are rapidly and inevitably eliminated (selected against) in the organisms of recipients or their contacts

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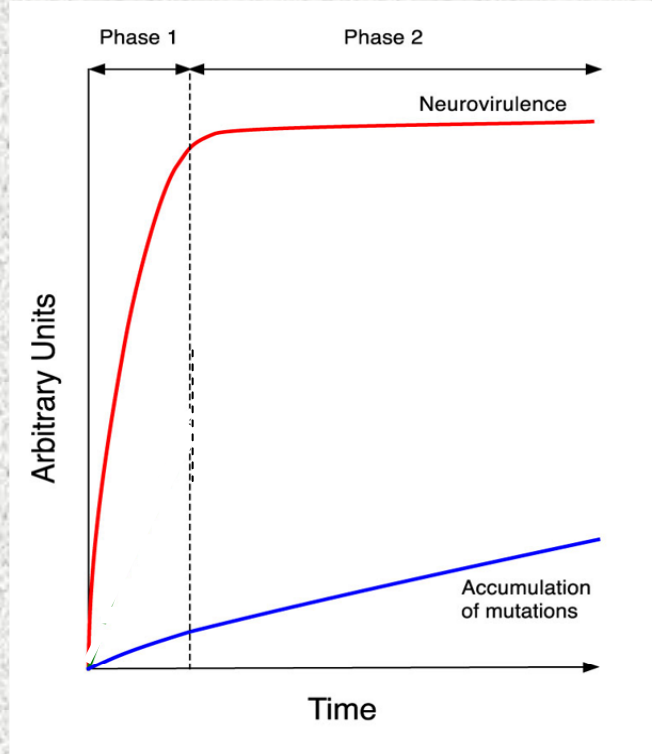
As a result, evolution of OPV derivatives follows a two-phase kinetics, with restoration of neurovirulence occurring very rapidly

Although OPV is less transmissible compared to wt parent (due to a lesser fitness), loss of attenuating mutations results in restoration of transmissibility



Corollaries:

(i) Although OPV is very efficacious, its decreased fitness may be an obstacle for reproduction in vaccinees under some conditions (e.g., in tropical countries),

(ii) OPV is acceptably safe when it cannot circulate freely, i.e., if populations surrounding its recipients exhibit relatively high herd immunity

or

when all susceptibles are immunized simultaneously

(ii) In populations with low herd immunity, where OPV can circulate and acquire wt-like phenotype (e.g., after stopping immunization), OPV is potentially as dangerous as wild polioviruses

To warm up the discussion…

When is OPV efficacious and when is it not?

It is efficacious, if used properly
Except in some tropical countries with poor sanitation

The real cause of the failure is unknown

interference from other viruses due to OPV low fitness?

Corollary:

Research aimed at elucidation of this problem is urgently needed

Efficiency of OPV reproduction in vaccinees in the "stubborn" regions should be investigated

Perhaps vaccination tactics should be changed

What is the reason for vaccine-associated poliomyelitis - vaccine reversion or exceptional host susceptibility?

Likely, exceptional susceptibility

possible contribution of discordant time-courses of virus reversion and development of immune response

Corollaries:

VAPP-inflicting capacity is an intrinsic property of OPV

It can be eliminated by vaccine improvement –

theoretically possible but hardly feasible practically

(to be discussed at another session)

Do evolved OPV derivatives (VDPVs) significantly differ phenotypically from wild polioviruses?

No

Corollaries:

Eradication of just wild polioviruses is not a critical issue, if vaccine derivatives are continuing to circulate

Certification of this achievement does not make much sense

Nigerian experience shows that the "1% divergence" criterion for VDPV is not warranted

What is the nature of cryptic circulation of VDPV?

Generally, the same as circulation of wild type virus in populations with a relatively high level of immunity

Corollary:

Cryptic OPV derivatives do, and will, exist until OPV is used and for years beyond
and
they may be the source of virus reintroduction into poorly immune populations

Under what conditions, and why, is OPV dangerous?

When OPV derivatives can freely circulate through large nonimmune populations

Corollaries:

Until there are overt, cryptic, or potential sources of poliovirus (wt or vaccine-derived), human populations should not be left unprotected

Paradoxically, this means that OPV use should not be discontinued in foreseeable future

(to be discussed at another session)